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Archiv fur pathologische Anatomie und Physiologie und fur klinische Medizin (Archive for pathological anatomy and physiology and for clinical medicine) - Vol. XCVI (Ninth Series Vol VI), No. 2. 1860

X.

On a Fungus Disease in Daphnia. Contribution to the Teachings on the Struggle of Phagocytes against Causers of Disease, by

Elias Metschnikoff in Odessa

The water fleas or daphnia, which are frequent everywhere, appear to be quite particularly suited to the study of several pathological processes which are in a position to shed a certain light on quite common problems of medicine. Although these crustacea, because of their very small body size and their delicate nature, are very inappropriate for all kinds of artificial contacts, they provide very good advantages for the investigation of such disease phenomena to which they are spontaneously subjected. As relatively small and rather transparent animals they can be observed uninterruptedly for several hours without suffering any damage and also studied further from day to day.

It has already been noticed by several researchers that the daphnia are often infested by various parasites which belong to the lowest organized plant and animal groups. Thus, Leydig * mentioned at least six diseases which are produced in part by coccidea (Psorosperms) and gregarine-like creatures, in part by actual fungi. Some of these diseases have been observed in more recent times by Claus** and Weismann***, but since that they have no longer been researched.

The disease which I will describe in the following lines as a fungus disease or simply as a yeast disease has, as far as I know, not been seen by any previous observer. I myself was completely unaware

* On the knowledge of the organs and the finer construction of the daphnides. Zeitschrift f. wiss. Zool. Vol XXVI, 1876, p.388.

** Contributions to the natural phenomena of daphnia, Zeitschrift f. wiss. Zool. Vol. XXXII, 1880, p. 188, and following.

*** Natural history of the daphnia, 1860, pp.78 and following, Archiv f. Pathol. Anat. Vol XCVI, No. 2.

of it while I was investigating pebrine*in daphnia two years ago. I found it first in spring of last year in an aquarium in which numerous Vallisneries and daphnia magna made up practically the entire flora and fauna. Among the daphnia my attention was drawn to several samples because of their white coloring. For that reason I considered that they were suffering from pebrin disease. The microscopic study showed immediately that it was a matter of an entirely different disease. All of the abdominal cavity up into that of the last antenna member was filled with massively accumulated fungus cells which turned out to be various stages of one and the same type of fungus. The latter, which I would like to introduce into science under the name Monospora bienspidata, is a genuine fungus and is composed of asci which form conidia and spores or house them.

The simple conidia appear in the shape of oval, straight (figs. 1 and 2) or slightly bent (fig. 3) pale cells which in any event coincide with the corresponding shapes of many other yeast fungi. They multiply through gemmation which is started up by the formation of very small button-like projections (figs. 4 and 9). Once the buds reach their final size equal to that of an adult cell it falls off from the same or remains connected to it. In the latter case there occur entire colonies of yeast conidia (fig. 11) which are held together only loosely in it so that when the sick daphnia are pulled to pieces the individual cells are released from the connection. In the great majority of cases the gemmation occurs on one end of the conidium. Exceptionally, however, the buds also form on the sides of the same, whereby the expanded conidium exhibits a corresponding knee-shaped bending (figs. 10,12, 13). At times I encountered tied-up cells as if they wanted to multiply by means of transverse spacing (fig. 7). In that time I was not able to note such a way of multiplication. The loosened conidia expand by a multiple whereby they then change their oval shape into a stick shape (fig. 14,15). In their further growth they assume a characteristic club shape (fig. 16) and then proceed to assuming a spore formation. Inside of the wider end of the club there occurs a thickening of the protoplasma (fig. 17) which expands gradually to the smaller pole so that lastly a nail-shaped spore is produced inside of the cell which has become an ascus. It is worthy of note that beside the end of the spore, which is situated in the wider cross section of the ascus, we always encounter an extremely small nucleus which has its focus either tightly against the spore or separated from it (fig. 18, 19).

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* Incidentally, I would like to point out at this time that pebrine is in no way a fungus disease. My investigations confirmed the opinion of Cornalia and Leydig according to which the pebrine parasite is a psorosperm. It is composed of amoeboid, laterlapped protoplasma formations in which the spores occur through endogenous formation. Hopefully, I shall be able to discuss this disease in greater detail some other time.

It becomes immediately evident from the described properties of the parasite that it exhibits the greatest similarity to the customary yeast fungi, even though its actual position in the fungus system has still not been ascertained, particularly since we know from the newer investigations by Brefeld* that yeast forms represent stages of very different yeasts (ustilaginea, tremollinea, etc.). Through the formation of asco spores our form approaches in the innermost of the sacharomyces in the sense of Reese, but I believe that they should be classified into a special species since (apart from the deviating way of life to which, however, no great significance is to be ascribed), they are also characterized by a unique needle-shape of the ascospores. It should also be pointed out that although other yeast fungi also only produce one spore in an ascus (as for example was indicated by Reess** for sacharomyces Pastorianus and mycoderma), this case does not present a rule for them, while I did not find more than one spore in thousands of asci of the menospora.

The yeast forms of other parasitic fungi differ from the monospora chiefly by the fact that they do not produce any asco spores, for which reason they cannot be brought into such a close relationship with the genuine yeast fungi. An exception to this is only the form which was found by Butschli.*** in a free-living nematode tylenchus pellucidus which produced both germ-forming conidia and rod-shaped asco spores. The similarity with the parasites of the daphnia is so considerable that I do not hesitate to also include the fungus of the tylenchus as a monospora.

All of the stages of the monospora which I examined are common in the abdominal cavity of sick daphnia. In the early stages of the sickness we only find budding conidia, whereas in the later days the asco spores prevail. Despite numerous investigations I have still not been able up to now to cultivate the fungus in question in an artificial medium. Acidified meat broths, apple juice, etc., were used by me as feed fluids.

In the daphnia which died from fungus disease we find large quantities of the spores which were shut into their asci and which are shallowed up by healthy individuals. Since the asci do not burst in the water, but the spores, on the other hand, which are so often found in the intestinal tract of the daphnia, are largely free of them, I believe that this is accomplished by the action of the gastric juice of the water fleas. As a result of the peristaltic the spores which are extremely sharp on both ends (hence the species designation of bicuspidata) penetrate partially into the intestinal wall and partially,

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* Botanical investigations on yeast fungi, Leipzig 1883

** Botanical investigations on alcohol-fermentation yeasts. Leipzig 1870, p. 83, table II, fig. 13

*** Studies on the initial development processes of egg cells, etc. Frankfurt, 1876, p. 148, table XIV, fig. 8.

however, into the abdominal cavity of the animal. We can observe such spores very often which are prevalent only in part in the abdominal cavity, whereas their greater portion remains hidden in the intestinal wall or in the intestinal cavity (figs. 25,32,33). Hardly did a piece of the spore appear in the abdominal cavity than one or blood corpuscles* became firmly attached to it in order to initiate the struggle against the intruder (fig. 25). The blood cells settle so firmly on the spores that they are torn away only seldom by the blood stream (fig. 26). In this case they are replaced by new blood corpuscles so that finally in the majority of cases the spores are surrounded by them more or less completely. Often the spores penetrate completely into the abdominal cavity, whereby they become the victims of the blood corpuscles. The number of the latter which gather around a spore varies very much, by the way, as can be seen when comparing figures 27,28,29, 32, and 31. When several spores are found next to one another in the abdominal cavity then there forms around them such an accumulation of blood cells that the entirety presents a true picture of inflammation (fig. 30) to the extent that such a picture can occur in an animal without vessels.** The blood corpuscles which gather around the spores do not always retain their independence since occasionally combine into a more or less extensive plasmodium (a so-called giant cell) (fig. 31).

Although the spores can reach the abdominal cavity from all of the parts of the middle intestine (except for the horn-shaped blind sack), this occurs chiefly, however, on both curves of it the first one of which lies at the start of the so-called "stomach" and the second one in the abdomen. We also find many spores, which are mostly completely intact in the intestinal contents or feces which indicates that they can bear the action of the gastric juices without incurring in any harm. After the spores has been lying for some time in the middle of a number of such cells it begins to experience very regular changes. First of all it thickens, takes on a light yellow color and maintains jagged contours (fig. 35). Then it swells at several places to various large, round or irregularly shaped balls (fig. 38-40), which take on a brownish-yellow color while the remaining part of the still rod-shaped spore appears to be lighter and yellower; still further, the entire spore crumbles into irregular brownish yellow, dark brown and almost black large and small nuclei (fig. 41,42). Its relationship to

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* I do not need to particularly point out that in daphnia, as in the case of invertebrates in general, the blood corpuscles are colorless amoboid cells which are suitable for accepting solid substances. They spin around in a system of lacunae and are brought into circulation by means of a hose-shaped heart; the daphnia are completely lacking in blood vessels, with the exception of a short outlet pipe which has been designated as an aorta by several authors.

** Also see my paper on intracellular digestion in Claus's works of the zoological institute in Vienna, vol. V, No. 2, 1883.

the earlier fancy spores can only be determined through the knowledge of all of the transitional stages. In the meantime the blood corpuscles combined into a fine-grained pale plasmodium which has retained still the capability of moving in an amoeba-like fashion (fig. 35-42). From time to time we find on certain places of the daphne's body entire batches of such plasmodia which are particularly conspicuous from the granules which are contained in them. This is also confirmed by the observations of daphnia which yielded the opinion expressed by me and by several other researchers concerning the formation of the so-called giant cells or mesoderm plasmodia through the merging or coalescing of ameboid cells and foreign objects.

For the following reasons I also believe that the observed changes which the spores undergo are to be considered as the result of the action of the blood corpuscles. When a spore, about half of it, remains for a long period of time in the intestinal wall and only a part of it is occupied by the blood corpuscles then the latter alone undergo the regressive transformation or the definitive decomposition whereas the section lying in the wall completely preserves its normal behavior (fig. 36,37). Such examples are too frequent for us to be able to doubt their legitimacy. Also serving as a further confirmation are those spores which have made a path for themselves partially outwards (fig.43) or in the thoracic cavity and another part of which are encompassed by the blood corpuscles, since in this case only the latter spore section changes. I would like to mention in passing that it is not at all rare for a spore which is complete, still unchanged or already somewhat attacked, to pass outwards through the wall of the animal's body.

From what has been said it is evident that the spores of the parasite which have reached into the abdominal cavity are attacked by blood corpuscles and probably killed through some current secret and brought into decomposition, that, in other words, the blood corpuscles have the task of protecting the organism from infectious materials. Nevertheless, this does not always occur in this way. In the cases when too large a quantity of spores reaches into the abdominal cavity of the daphnia, as in the example which is given in fig. 32, or where for other reasons one or more spores remain untouched by the blood corpuscles (fig. 34) we come to the breaking out of the disease. The spore which has remained free reaches the germ. It drives on one side a small hill-shaped projection (fig. 44) which soon produces a round bud (fig. 45). The latter changes into an oval conidium and falls from the hill or else remains attached to it. There then form more conidia which sometimes appear in small chains (fig. 48). The first sprout retains in individual cases its original insignificant size; in other cases, on the contrary, it grows in a sterigmen-like extension (fig.46-48) which exceptionally can exceed the length of the entire spore.

In such a way there now occur oval conidia which soon start to sprout and thus infect the organism of the daphnia more and more. The conidia are scattered in the entire abdominal cavity by the blood stream and are stored in such areas where the blood circulates the slowest, for example in the forehead and in the back parts of the mantle cavity,

in the vicinity of the tail appendage. In these places there consequently occur large heaps of fungus cells. The blood corpuscles do not behave passive in all this against the invasion of the conidia. They consume some of them in order to kill them in the inside of the cell body. Since these processes are much easier to follow in this case than in the case of the struggle of the phagocytes against bacteria I consequently would like to spend more time in describing my observations. In order to obtain sure results it is necessary to have the same object before one's eyes for several hours of time. Then we can see that the blood corpuscles really incorporate the conidia. This occasionally occurs very quickly and in other cases, on the other hand, it takes place very slowly. Very convenient for the observations are such double conidia one cell of which has already been eaten up and the other one of which, however, is still free (fig. 60). Then after some time has elapsed the other one will also succumb gradually to the protoplasma of the blood corpuscle (fig. 61). If the conidia has already expanded itself in the shape of a rod, then the blood corpuscle extends around it, whereby finally there occur spindle-shaped cells, which are frequently observed (fig. 64 to 66). Still longer conidia are attacked by one or more blood corpuscles (fig. 62) which reminds us of the conditions which are given for the spores above. The number of conidia which are consumed by a blood cell differs greatly. Normally we only find a pair of conidia in each cell. In some cases, however, three, four and more conidia can be eaten up (fig. 59,63).

The blood corpuscle which eats up the parasitic conidia through its ability to move also remains capable of movement even after devouring the foreign body, as we can see from the comparison of the pictures which are taken of one and the same blood corpuscle in intervals of ten minutes each (fig. 42-52). On occasion the conidia-containing blood cells melt into small plasmodia (fig. 57) which then accommodate more parasites in its inside.

The conidia which are incorporated do not remain intact in the body of the blood cells. They are regularly killed which can be noticed from the contours which have become much sharper and the habitus of the conidia which has collapsed more (fig. 49-57). In order to convince myself even more I observed for several hours at a time such conidia which had been consumed within the scope of the sprout formation. I was never able to note the continuation of the gemmation in the inside of the blood corpuscle. Figs. 69-71 show us a blood cell a which was found in the inside with a sprouting conidium. Between the conditions of fig. 68 and 71 there occurred an interval of three and three quarters hours during which time the conidium bud in no way changed while the two free uneaten conidia c and d had enough time to propel new buds. If it thus cannot be doubted that the consumed conidia are dead it nevertheless remains to be seen whether or not they were consumed in the live state. Although it is not very likely that a budding conidium dies out by itself, I still have on the other hand direct observations that support the fact that the blood corpuscles are able to consume live fungus cells. Thus, the conidia which are shown in figures 58 and 66 present entirely normal patterns in all regards. I could only notice

in the inside of the phagocytes some fungus cells which could be considered as dead (because of the sharpness of the contours and the other characteristics). It would also have been impossible to claim that the spores which are surrounded by the blood corpuscles were already previously dead and were not fit for germination, that the phagocytes are altogether not in a position to be able to consume live fungus spores or conidia. When in general we must also admit that among fungus spores there are also often such which do not germinate for unknown reasons then everyone knows who has raised fungi that the percentage of such spores in relation to those which are surrounded and changed in the daphnia body by the phagocytes becomes gradually smaller. Apart from these reasons, I have directly ascertained that budding spores can also be attacked by blood corpuscles. Thus, in fig. 33 I have illustrated such a spore which was touched by a blood cell only after the formation of the sterigmen-like hill, whereby the bud still has not been surrounded by the protoplasma.

We thus reached the conclusion that the blood corpuscles are really able to subdue living yeast fungi or spores. While, however, the latter experience the above-described reformation, the consumed conidia do not show us any changes of that kind. Instead of that they become continuously thinner and more refractive. Large vacuoles also often form around them (fig. 55) which are very similar to those which occur in the protozoa body around the bit of food. The difference between the change in the spores and the change in the conidia could be explained by the different properties of the cell membranes.

If it is true on the one hand that the conidia are pursued by the blood cells then on the other hand it is not to be doubted that the latter are also afflicted by the parasites. A few times I saw, for example, that the fully consumed blood corpuscle burst into several bits in front of my eyes whereby the conidia freed themselves from the cell body (fig. 67). I was also able to see on several occasions that the blood corpuscles gradually dissolved in the vicinity with numerous fungus cells. This indicates that the conidia separate some kind of liquid which is damaging to the blood corpuscles. The last assumptions become the more palusible since it is already known that the conventional yeast fungi also act as a poison to many animals. The infected conidia can also dissolve such blood cells which had previously collected about a spore, as is shown in fig. 73. Here we find in the center a spore which has already changed considerably and around which the remaining part of the blood corpuscle and expanded conidia are to be seen.

The more advanced the disease is the greater the number of blood corpuscles which are dissolved so that at the time when the daphnia contains a significant number of mature spores it already shows no or only a few blood corpuscles.*

* A new formation of blood corpuscles or a division of them could not be noted by me during the entire disease.

Besides the blood corpuscles there are only the isolated connective tissue cells of the daphnia which play a similar role as phagocytes (eating cells). They behave as a whole quite similarly to the blood corpuscles in that they also eat the fungus cells (fig. 74). They are also released in the same way by conidia so that in later stages of the disease all of the phagocytes disappear from the daphnia. Other tissue elements do not suffer such a considerable loss. Thus we often see a large number of conidia developing on the heart muscles, despite the fact that the heart continues uninterruptedly with its contractions. The most minute fibers which we can see in the mantle also remain apparently completely intact.

When the daphnia first becomes sick, that is to say when conidia have appeared in it, then, as far as I have seen, it is completely destroyed without hope of salvation. In the last period of the disease, when many spores have formed, it assumes a diffuse milky white color. The movements also remain brisk as in a healthy specimen and the heart, although often overloaded with spores, contracts in an apparently completely normal manner; the intake of food continues even up into the last few days before the death. The entire disease lasts over two weeks. Thus, a young daphnia which I isolated at the start of the conidia formation died on the 16th day.

It is not at all a rare thing for the yeast disease occurs together with the pebrine in one and the same individual, but the two diseases do not show any signs of developing otherwise than in their usual manner.

From what has been said we can see that the infection and the disease of our daphnia is composed of a battle of two living beings - the fungi and the phagocytes. The former present us with lowly organized single-cell plants, the latter, however, the lowest tissue elements which show the greatest similarity with the simplest organisms (amoeba, rhizopods, etc.). It should, however, be noted that the nuclei of these elements are so unfavorable to observe that we cannot attach too much value to negative findings. The phagocytes, as the original property of the intracellular food intake is retained act by means of same as an exterminator of the parasites and thus appear as the carriers of the healing forces of nature which have been known since a long time ago and which were first removed by Virchow in the tissue elements. The basic concept of the cellular pathology of this master also corresponds to the overall development of the daphnia disease, although here the primary role is referred to precisely as the most independent tissue elements.

It has already been shown above that the outcome of the struggle differs. When it is a matter of the killing of the spores then the phagocytes have the upperhand in the majority of cases so that they appear to be extremely suitable as prophylactic organs. Things occur quite differently in the cases where the disease has already broken out, since here the

parasites control the field of battle. From this we can already see that the phagocytes are much better suited for the battle against spores than for the battle against the highly proliferating conidia, which should already have to be expected a priori. In order to obtain for myself a better idea of the quantitative conditions of this battle I undertook the following. I investigated 100 individual specimens of daphnia from the aquarium in which the yeast disease had broken out. I divided them into three categories, according to the most accurate microscopic investigation: (1) into entirely healthy ones, that is to say those which had neither spores, nor conidia of monospora in their abdominal cavity, (2) into sick ones, that is to say ones which contained conidia, and (3) into infected ones, that is to say those which had spores in their abdominal cavity which were surrounded by phagocytes. The results which were obtained in this way were summarized by me in the following table.

Length of the body in mm	Entirely healthy			sick			infected			Total
	male	female	all	male	female	all	male	female	all	
1.33-1.50	2	2	4	-	3	3	1	3	4	11
1.51-2.00	1	13	14	4	4	8	16	24	40	62
2.01-2.50	1	3	4	-	3	3	2	6	8	15
2.51-3.23	-	5	5	-	-	-	-	7	7	12
TOTALS	4	23	27	4	10	14	19	40	59	100

It is evident from these numbers that out of 100 daphnia which were living in an infected aquarium for over 2 months only 14 became sick, while as a whole 73 individuals (14+59) became infected, 50 out of which were freed from the infection substance through the prophylactic role of the phagocytes. That they were actually healthy is verifiable from the fact that I placed them into isolated glasses where there was no chance for a reinfection to occur. Thus at this time I have a very active medium-sized daphnia which I found 23 days ago with many spores in the abdominal cavity which were surrounded by phagocytes. I then isolated it. Three days ago it gave birth to three healthy youngsters. In another glass I also kept another infected female for 19 days. It remained quite healthy and is bearing three entirely normally developed embryos in the thoracic cavity.

We can also see from the table that the yeast disease preferably attacks young daphnia, while adult individuals, although also capable of becoming infected, usually do not become sick. They appear, according to my opinion, to be much more susceptible to pebrine. The youngest recently born daphnia also do not become sick, apparently since they have not as yet taken any food and therefore have not had the occasion to eat up any infected spores.

As I have mentioned at the beginning, the fungus disease of the daphnia presents a certain interest to us because it helps us to obtain some closer information on some pathological phenomena in higher animals. Thus, for example, this strengthens the concept that the white corpuscles and other phagocytes of vertebrates consume the producers of the sickness in general and the fission fungi in particular,*, whereby they provide a considerable service to the organism. The more certainly we could raw this conclusion from the total sum of these experiences the more impossible was it up to now to directly follow on a definite specimen the entire process of the eating up of yeast fungi by phagocytes and the further developments of same. Therefore at the present time it is possible for us to more definitely criticize the data according to which the bacteria in white blood corpuscles was conceived of in an entirely different way. Thus, R. Koch** pointed to the fact that he put forth that the blood corpuscles of septicemic mice contain a different quantity of bacilla so that the fission fungi break into white corpuscles and multiply in them. He was, however, not able to directly report on the process of the breaking in and the subsequent multiplication since in such cases it is not possible to observe the object under normal circumstances, We investigate either a drop of escaped blood or preparations which had previously been treated with reagents. It seems to be much more probable, however, that also in these cases, just as in the fungus sickness of daphnia, the parasites are consumed by the blood corpuscles and that when the latter consume too many vacilla they finally fa-l apart and decompose, whereby the fission fungi are released. The mice septicemia thus has another particular similarity with the fungus disease as in both cases, despite the consumption of the parasites by the phagocytes, the former win the upperhand and are victorious probably because of the reason that the introduers multiply too greatly and perhaps also separate a poisonous substance. Equally interesting is another example reported on by Koch*** where the phagocytes occur as the winners. Thus I would like to confirm at least the fact enunciated by the mentioned researchers that the frogs which have been infected with anthrax remain immune and that at the same time bacilla-containing cells are found in them. The nature of the latter is not defined more closely and unfortunately it is also not given whether the cells are amoeboid so that we can only state as an assumption that we

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* See the Bioligische Zentralblatt, Vol. III, No. 18, 1883, p.562

** Investigations on the etiology of wound infection diseases, Leipzig 1878, pp.44,72

*** The etiology of fungus disease in Cohn's contributions to the biology of plants, Vol. 2, 1878, p. 300, table XI, Fig. 3.

are dealing simply with white corpuscles. They contain, besides the usual bacillae, spiral-twisted leptothrix tissues which have grown out from such bacillae. Koch said that: "The fact that the bacillae which are taken up by the cells as short rods grow in them and, after they have filled the inside of them under the formation of various kinks and bends, finally burst follows from the fact that besides the free bacilla-spirals and bndles we find coincident and empty cell membranes as the last remains of the disrupted cells". Sinde this result was achieved on drops which were extracted from the frog and transferred to the object carrier, it is much more probable, in my opinion, that fully consumed phagocytes thereby burst, which, by the way, they also do very easily. The long fiber is probably consumed as such and placed in the spiral form in the swallowing. I am permitting myself to express these assumptions at this time not only because of the reason that they are in much greater harmony with the direct findings on daphnia but also because of the situation that it would otherwise be very diffult to explain why the frogs remain insensitive to anthrax when the bacteria of anthrax find a very favorable environment for their development in certain -rog cells. I am much more of the opinion that in this case the bacilli are destroyed by phagocytes whereby it also is not excluded that they are also hindered by other factors in their development.

The significance which Koch* gives to his findings of tuberculous bacilli in large cells conforms much more to the concept that I am defending here. He assumes that the younger large cells contain living bacilli whereas in the older ones they have already died out. This is in complete agreement with my results obtained on daphnia and can simply be formulated in that ~~alrge~~ cells eat up bacilli and then kill them. That the definite victory of the phagocytes does not necessarily follow as yet is evident.

When we assume the opinion that the phagocytes fight directly against disease viruses then it becomes understandable that the inflammation exerts a harmful effect on the bacteria invasion. The last theory, which has been accounted for for a long time in medical practice, has already been carried over into the textbooks. In recent times, it has been once more defended by Buchner** who, supported by special experiments, ~~represented~~ the thesis that "the inflammation process could express a harmful effect only on the fission fungi present in the tissue", that consequently "the inflammatory change of the tissue appears as the natural, suitable reaction of the animal organism against fission fungi resulting in healing". We can support these assumptions with much more assuredness if we assume that the essential factor of the inflammation lies precisely in the gathering together of the phagocytes and that the latter thereby simply eat up the irritant, that is to say in other words that the inflammation

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* Die etiology of tuberculosis. Berliner klinische Wochenschrift, 1882, No. 15, p. 222.

** The Nagel theory of infection diseases, etc. Leipzig, 1877, and the Etiological Therapy and Prophylaxis of tuberculosis of the lungs, 1883, p. 16 on.

only represents a special case of intracellular food intake, as I attempted to prove based on comparative pathological observations. My experiments on daphnia can be used as a further support for this theory. The total fight between monospora and phagocytes is to be conceived of as a kind of diffuse inflammation, a hemitis. When the needle-shaped spores concentrate in a larger amount on a certain point (fig. 30) then we have a localized phagocyte gathering which is quite similar to the one which occurs after an injury. When a larger number of daphnia are sampled through we find such individuals whose bodies exhibit small wounds. These wounds, probably caused by bites from other animals, are usually septic and contain, in addition to bacteria, also a brown detritus mass (fig. 76). On the inside of the wound the blood corpuscles which flow by collect into considerable masses, as I have described for other vertebrates. Before, however, the detritus can be absorbed by the latter the wound becomes covered by a rapid epidermis neoplasm whereupon the phagocytes once more break up. Very similar occurrences can be observed in the frequent cases when the daphnia skin is somewhat burst open through the pressure of the inflammation. There immediately form around the damaged spot several blood corpuscles which are soon followed by others so that a temporary phagocyte accumulation occurs here (fig. 75).

Since it has been pointed out that in its essence the inflammatory reaction is a very old device in the animal kingdom which has its foundation in the digestion mechanism of the one-celled organisms and the lowest metazoa (sponges) then perhaps there is a prospect of making clearer the very obscure phenomena of immunity and vaccinations through analogous conclusions with other phenomena of food intake and digestion. It will also perhaps be possible at some time to conveive of some temperature phenomena of fever, if we hold this to be a healing reaction of the organism with Pfluger and his school of thought, as a useful device for increasing the activity of phagocytes. If this is related to the still-too-little-known phenomena then we can still reach the general conclusion that the pathological results which are obtained on lower animals can be considered as a whole to be a new support for the basic idea of cell pathology.

Explanation of the illustrations

All of the illustrations, with the exception of figures 68 and 71, were formed with the aid of the Nachet drawing prism.

Fig. 1-14 Conidia of monospora under various conditions. Enlargement Ocular 4, System 9 (dry) of Hartnack

Fig. 15-16 Extended conidia preparing for spore formation. 4+9

Fig. 17-19 Formation of the ascospore. 4+9

Fig. 20-23 Blood corpuscles of daphnia magna, drawn after life. 4+9

Fig. 24. A blood corpuscle treated with acetic acid. 4+9

Fig. 25 A spore which penetrated into the abdominal cavity through the intestinal wall and surrounded by four blood corpuscles, m muscular layer of the intestine, b epithelical layer of the same, s rod layer. 4+7

Fig. 26 Another spore in a similar condition. 4+7

Fig. 27 A spore, surrounded by blood corpuscles, from the abdominal cavity of a daphnia. 4+9

Fig. 28 Another spore after treatment with acetic acid. 4+9

Fig. 29 The abdomen of an infected daphne with several spores, surrounded by blood corpuscles, in the abdominal cavity. Many spores are also situated in the intestinal wall and in the intestinal lumen. 3+4

Fig. 30 A piece of the abdomen of another daphne with considerable phagocyte accumulation around the spores. 4+7

Fig. 31 A blood corpuscle wrapping around a spore. 4+9

Fig. 31 A blood corpuscle wrapping around a spore. 4+9

Fig. 32 A piece from the front part of the body with many spores emerging and surrounding. a= germinating spore. 2+7

Fig. 33 The spore a with the bud and a blood corpuscle adhering at 4+9

Fig. 34 A piece from the front part of another daphne, 4+7

Fig. 35-42 Various stages of the changes undergone by spores under the effect of the phagocytes. Fig. 35 plotted at 4+9, the rest at 4+7.

Fig. 43 A spore which has partially gone out of the skin. a = the small skin wall, b= the lower spore part which is surrounded

by the blood corpuscle and greatly changed; 1 young leptothrix which has settled on the free part of the spore. 4+7

Fig. 44 A budding spore. 4+9

Fig. 45 The same five hours later. 4+9

Fig. 46-48 Other stages of the conidium formation. 4+9

Fig.49-52 One and the same blood corpuscle in four different stages of movement. 4+7

Fig. 53 A phagocyte which has consumed two fungus cells. 4+9

Fig.54-56 Another blood corpuscle containing conidia. 4+7

Fig. 57 A phagocyte plasmodium containing a fungus cell. 4+7

Fig. 58 A blood corpuscle in close contact with two conidia. 4+7

Fig. 59 The same a half an hour later. 4+7

Fig. 60,61 Two eating stages of one and the same blood corpuscle. 4+7

Fig. 62 A fungus cell touched by two blood corpuscles. 4+7

Fig. 63 A completely consumed blood corpuscle. 4+7

Fig.64-66 A blood corpuscle in three moments of the surrounding of a conidium. After a short stay, the cell a has once more departed. 4+7

Fig. 67 A burst blood corpuscle from which the conidia have released themselves. 4+7

Fig. 68 Two blood corpuscles one of which (a) has consumed a budding conidium, while the other one (b) touches two conidia (c,d)

Fig. 69 The same figures a half an hour later. The conidium d has begun to bud.

Fig. 70 The same figures, with the exception of the blood corpuscle b which has departed in the meantime, two hours later than fig. 69. The conidium e is at the start of the budding stage.

Fig. 71 The same figures five hours later than fig. 70

Fig. 72 Two blood corpuscles in the vicinity of four conidia. 4+7

Fig. 73 A group of conidia which has broken up the blood corpuscle housing a spore; an empty bubble and fine detritus have remained as residue. 4+7

Fig. 74 A connective tissue phagocyte containing three fungus cells. 4+9

Fig. 75 A wounded piece of skin of a daphne with many blood corpuscles, b=bacilli. 4+7

Fig. 76 A burst piece of skin of another daphne also with many blood blood corpuscles. 4+9.

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